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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/756,830	01/08/2001	Sydney Brenner	5525-0046.30	6856

22918 7590 05/04/2006

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EXAMINER	
SISSON, BRADLEY L	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 05/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/756,830	BRENNER ET AL.	
	Examiner	Art Unit	
	Bradley L. Sisson	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 January 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,6,7,15 and 16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,6,7,15 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-4, 6, 7, 15, and 16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. As set forth in *Enzo Biochem Inc., v. Calgene, Inc.* (CAFC, 1999) 52 USPQ2d at 1135, bridging to 1136:

> To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.' " *Genentech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997) (quoting *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)). Whether claims are sufficiently enabled by a disclosure in a specification is determined as of the date that the patent application was first filed, see *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986).... We have held that a patent specification complies with the statute even if a "reasonable" amount of routine experimentation is required in order to practice a claimed invention, but that such experimentation must not be "undue." See, *e.g.*, *Wands*, 858 F.2d at 736-37, 8 USPQ2d at 1404 ("Enablement is not precluded by the necessity for some experimentation . . . However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' ") (footnotes, citations, and internal quotation marks omitted). In *In re Wands*, we set forth a number of factors which a court may consider in determining whether a disclosure would require undue experimentation. These factors were set forth as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *Id.* at 737, 8 USPQ2d at 1404. We have also noted that all of the factors need not be reviewed when determining whether a disclosure is enabling. See *Amgen, Inc. v. Chugai Pharm. Co.,*

Ltd., 927 F.2d 1200, 1213, 18 USPQ2d 1016, 1027 (Fed. Cir. 1991) (noting that the *Wands* factors "are illustrative, not mandatory. What is relevant depends on the facts.").

3. For convenience, claim 1 is reproduced below.

1. (Currently amended) A method of synthesizing a repertoire of oligonucleotide tags, each having a predetermined length in the range of from 18 to 60 nucleotides, the method comprising the steps of:

(a) providing a repertoire of same-length oligonucleotide tag precursors in an amplicon, wherein said amplicon is a cloning vector, and wherein each oligonucleotide tag precursor consists of one or more words, and each word is an oligonucleotide having a length of three to fourteen nucleotides, selected from a minimally cross-hybridizing set of oligonucleotides, such that a duplex consisting of a word of the set and the complement of any other word of the set contains a number of mismatches that is either 1, 2 or 3 less than the length, in nucleotides, of the word;

(b) cleaving a first aliquot of the amplicon to produce a first opened amplicon and a first fragment, said fragment containing at most one word from said oligonucleotide tag precursor;

(c) cleaving a second aliquot of the amplicon to produce a second opened amplicon and a second fragment, said fragment containing one or more words from said oligonucleotide tag precursor;

(d) ligating said second fragment containing one or more words into said first opened amplicon, thereby elongating said oligonucleotide tag precursors in said first aliquot of the amplicon;

(e) amplifying the elongated oligonucleotide tag precursors in said first aliquot of the amplicon; and

(f) repeating steps (b) through (e) until a repertoire of oligonucleotide tags having the predetermined length is formed.

4. In accordance with the amendment method, one is to cleave at most one word from an "oligonucleotide tag precursor," which is a part of "a cloning vector." As set forth in said method, the "cloning vector" is to comprise "a repertoire of same-length oligonucleotide

precursors," such that "a word of the set and the complement of any word of he set contains a number of mismatches that is either 1, 2, or 3 less than the length, in terms of nucleotides, of the word."

5. In view of the foregoing, one could cleave a word from the cloning vector that is simply a 3mer, and for which no nucleotide is complementary to the associated strand. Further, one may cleave additional words, and they too need not be complementary to their antiparallel strand.

6. The specification is essentially silent as to how one would cleave 3mers, or any other duplex oligonucleotide, when the same duplex structure comprises such a large percentage of mismatches. Indeed, the specification is essentially silent as to providing any guidance as to how one would fashion and amplify such a cloning vector.

7. While claim 3 requires the use of a Type IIs restriction endonuclease, it is noted that type IIs recognize non-palindromic sequences and cleavage occurs outside of the recognition site. As presently worded, the method pf claim 1 requires one to use a "cloning vector," which has been construed as encompassing plasmids, which exist as a loop, or are circular in nature. By using a type IIs restriction endonuclease, one would achieve a cut several nucleotides outside of the recognition site. It is significant to note that by cutting the cloning vector but a single time, all one would achieve is an opened vector. No fragment/word/oligonucleotide would be generated. The cutting of a second aliquot of the same vector/plasmid with a type IIs restriction endonuclease would have the same end result.

8. Even if the cloning vector did comprise multiple words, and there was a type IIs restriciton endonuclease recognition site present, such an enzy, e.g., *Mbo* II, would cleave 8/7 nucleotides outside of the recognition site. Such cleavage is, however, dependent upon the two

strands of the vector being complementary, or to rephrase, not have the mismatches present, as is required of claim 1. Again, the specifiaiton fails to set forth the reaction conditions and starting materials necessary to arrive at the intended product.

9. Aside from teaching how to make the invention, the specification must also enable the use of the product so produced (and claimed). Said disclosure must also disclose the best mode contemplated by applicant for both the claimed method and the claimed product.

10. The specification provides the following examples:

a. Example 1, "Repertoire Synthesis by Repeated Cycles of Cleavage, Self-Selection, Ligation, and Amplification," pages 14-16;

b. Example 2, "Repertoire Synthesis by Convergent Assembly of Error-free Oligonucleotide Tag Precursors," pages 16-18;

c. Example 3, "Construction of an Eight-Word Tag Library," pages 18-24.

11. Clearly, the three examples do not each the skilled artisan how to recognize useful over non-useful oligonucleotides or vectors.

12. Assuming *arguendo*, that one of skill in the art could make a repertoire of oligonucleotide tags, the specification does not teach how one would be able to synthesize only useful oligonucleotide tags. Furthermore, the specification does not teach a reproducible and useful procedure whereby aid useful tags are recognized and used. The situation at hand is analogous to that in *Genentech v. Novo Nordisk A/S* 42 USPQ2d 1001. As set forth in the decision of the Court:

> " '[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation.' *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *see also Amgen Inc. v. Chugai Pharms. Co.*, 927 F. 2d 1200,

> 1212, 18 USPQ2d 1016, 1026 (Fed Cir. 1991); *In re Fisher*, 427 F. 2d 833, 166 USPQ 18, 24 (CCPA 1970) ('[T]he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.').
>
> *****
>
> "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. *See Brenner v. Manson*, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (starting, in context of the utility requirement, that 'a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.') Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.
> "It is true . . . that a specification need not disclose what is well known in the art. *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. <u>However, when there is no disclosure of any specific starting material or any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art.</u> It is the specification, not the knowledge of one skill in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research. (Emphasis added)

13. Accordingly, and in the absence of convincing evidence to the contrary, 1-4, 6, 7, and 15-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

14. Claims 1-4, 6, 7, 15, and 16 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

15. In order to satisfy the utility requirement, either the resultant product has utility or that the product's utility is derived downstream in its use in a method, which is recognized as satisfying the utility requirement.

16. Claims 1-4, 6, and 7 are all drawn to a method of synthesizing a repertoire of oligonucleotide tags. Claims 15 and 16 are drawn to said set of oligonucleotide tags. The specification has not been found to set forth a specific and substantial utility for the product and a review of the disclosure fails to find where the resultant and clamed product, when used, would in turn meet the utility requirements. Specifically, it is not enough that one can synthesize, or claim outright, a "tag" that could be used to determine if a complementary sequence is present, e.g., an expressed sequence tag or EST, a sequence for which no known utility exists. While the tags can be used to determine if a complementary sequence exists, all nucleic acids can be used in such a manner. While one may elect for that which exhibits less cross-hybridization, the intended target, even if unique, must have a specific and substantial utility. Simply determining its existence does not suffice.

17. The situation at hand is analogous to that of *In re Fisher* (CAFC, 04-1465, decided 07 September 2005). In *Fisher* the disclosure provided five ESTs and assertions as to their potential utility. Here, applicant is claiming a method of producing "tags" and the "tags" per se. Like *Fisher*, no evidence has been presented that the product of the claimed method or the product outright, does in fact have any of the alleged utilities. Further, the aspect of finding complementary sequences (which could be an EST) is not considered to be a substantial utility as the utility requirement is not satisfied for like the ESTs of *Fisher*, the product, even it had been produced/found, would be at best the subject of further research and development so to

determine if it does in fact have any real value. In view of the clear need for the product of the claimed invention to have utility, and no convincing showing has been made in this regard as to its satisfaction, no specific, substantial, and credible utility exists in readily available form a the time of filing.

18. Claims 1-4, 6, 7, 15 and 16 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Response to argument

19. At page 5, bridging to page 6, of the response received 26 January 2006, argument is presented that one of skill in the art would have known how to select for useful tags and would have also known how to make and use them.

20. This argument has been fully considered and has not been found persuasive. Attention is directed to MPEP 2145.

> Attorney argument is not evidence unless it is an admission, in which case, an examiner may use the admission in making a rejection. See MPEP § 2129 and § 2144.03 for a discussion of admissions as prior art.
> The arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997) ("An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a prima facie case of obviousness."). See MPEP § 716.01(c) for examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration.

21. It appears that applicant is attempting to satisfy the requirement of 35 USC 112, first paragraph, through obviousness. Obviousness, however, cannot be relied upon for satisfaction of 35 USC 112, first paragraph. In support of this position, attention is directed to the decision in *University of California v. Eli Lilly and Co.* (Fed. Cir. 1997) 43 USPQ2d at 1405, citing *Lockwood v. American Airlines Inc.* (Fed. Cir. 1997) 41 USPQ2d at 1966:

> Recently, we held that a description which renders obvious a claimed invention is not sufficient to satisfy the written description requirement of that invention.

For the above reasons, and in the absence of convincing evidence to the contrary, the rejections are maintained.

Conclusion

22. Rejections that appeared in the prior Office action and not repeated hereinabove have been withdrawn.

23. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

24. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

25. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571) 272-0751. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

26. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

27. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bradley L. Sisson
Primary Examiner
Art Unit 1634

BLS
17 April 2006